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Dear Kapp':

I was very glad to get a reprint of your review article on lead that was published recently by Granick, Sassa and yourself. This was very helpful in bringing me up-to-date on a subject that I took a fairly deep interest in a few years ago but have not been current on more recently.

At several places in the review there is the comment that more aggressive recourse might be made to chelation therapy. Do you know of any really searching evaluation, both theoretical and empirical, of this approach from the point of view of possible side-effects as well as efficacy? For example, I am somewhat concerned about the possibility of remobilizing lead that may be in various depots and at least hypothetically exacerbating an acute toxicity.

I was also interested in what new insight there might be in individual variation, and possibly genetic polymorphisms, in response to lead exposure. I am enclosing one reprint that seemed to conform with this expectation; but I have not seen much further work on the same question. I would have thought that, a priori, blood glutathione levels would have a good deal to do with the detailed transport of lead and your review gives some hints in that direction. The more recent work on metalliothionein was new to me; but as far as I could surmise, lead does not seem to be directly involved with it. Since so much lead is bound within the erythrocyte, it would seem to me that more work on the identification of the intracellular protein, and on differences in amount and binding capability of such an entity might help unravel some of the variability in individual response. Do you think that either the Barltrop or Kaplan groups are continuing their work on this entity.

With so many different possible compartments for lead, and the lack of much information about the movement from one compartment to another, it is surprising that total blood lead is much use at all as an index. We may not really have an informed, critical view about that until there are some possibly better hints from better defined compartments.

Again, the review did a great deal to clear up the gaps in my recent apprehension of the biology of lead and for that I am indeed * grateful. There is so much material to be covered, and much of this was necessarily condensed, that it seems like the subject might easily be worthy of a more comprehensive monograph. Or perhaps this is already being done elsewhere.

I also read over Dr. Jandl's statement. In many ways it is pathetic; and the more so since it offers very little by way of constructive advice on how to evaluate standards for lead hazard. He was doubtless reacting to the obtuseness that I'm sure was in the criterion document, and perhaps the sense that "erythrocytic protoporphyrin" was being used as an incomprehensible scare word - and there may even be some merit in that. However, I agree with you that it is unfortunate that the debate dips to this level and in other respects even worse.

Leaving aside his rather non-contributory critique, it seems we really are in a dilemma of some magnitude in trying to provide a rationale for lead standards: What should be perfectly obvious is that the present situation is intolerable, even if we perhaps do have to discover more relevant indexes of toxic burden.

Yours sincerely,

Joshua Lederberg

JL/gel

to you colleagues
+ yourself!